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Notification of a Family History of Breast Cancer: Issues of Privacy and Confidentiality

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Little information is available about notifying individuals with a family history of cancer about their risk of cancer. With the recent identification of *BRCA1*, an important predisposition gene for breast and ovarian cancer, genetic testing is becoming available to high-risk women and their families. Some of these individuals may not be aware of their family history and may be notified of their family history by medical personnel or biomedical investigators. This disclosure could be detrimental to the individual by changing their perception of risk, sense of privacy, or psychosocial well-being.

Members of 544 breast cancer families are currently being contacted as part of an epidemiologic follow-up study at the University of Minnesota. Some family members were unaware of their relative's diagnosis and therefore, notification occurred when they were contacted by study personnel. To determine the impact of risk notification in this context, 376 male and female relatives of 160 breast cancer probands were surveyed to assess their prior knowledge of their family history of cancer, issues relating to study participation, and their concerns regarding the possibility of developing cancer. Following a telephone interview about family history, family members were administered a short, open-ended questionnaire.

The majority of individuals (82%) were blood relatives of the proband and 71% were either first- or second-degree relatives. A proportion of blood relatives (24%) were not aware of their family history of breast cancer. More blood relatives (76%) than non-blood relatives (62%, $P < 0.01$) were aware of their family history. 43 respondents (12%) expressed specific concerns about participating in the large genetic follow-up study and 16 comments concerned privacy issues. Neither the reasons for participation nor an individual's concern about developing cancer was associated with gender of the respondent, relationship to the proband, or awareness of breast cancer in the family. Interestingly, individuals who were notified about their family history through the large follow-up study were no more likely than other family members to be more concerned about developing cancer.

Understanding the privacy and psychosocial issues of family members who are informed about a family history of breast cancer may aid in developing appropriate guidelines for notification. Risk notification in this setting does not appear to have a significant impact on these family members.

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INTRODUCTION

A family history of breast cancer is one of the strongest independent predictors for developing breast cancer [Harris et al., 1992]. As cancer susceptibility genes are identified, including *BRCA1* [Miki et al., 1994] and *BRCA2* [Wooster et al., 1994], genetic testing for breast cancer [King et al., 1993; Lynch et al., 1993] and various other cancers and conditions [Caplan, 1992] can be anticipated. The ethical and psychosocial implications of genetic testing will affect all areas of science, medicine, and the law. Before genetic testing is fully available, an evaluation of the effect the knowledge will have on individuals and families is required.

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A family history of breast or other cancer is currently one factor used to estimate the level of genetic risk for developing cancer. With the imminent development of molecular diagnostic tests for breast cancer [American Society of Human Genetics Ad Hoc Committee, 1994; Motulsky, 1994], accurate family history and pedigree information will be important. For individuals who are knowledgeable about their family histories, the availability of testing may offer reassurance or improve access to appropriate medical care [Biesecker et al., 1993]. However, some individuals are unaware that they have a family history of cancer and may learn of a relative's diagnosis from individuals outside the family. What impact will the disclosure of a family history of cancer have on an individual's perception of risk or psychosocial well-being? Will notification increase a person's general anxiety or worry about developing cancer? One guiding principle should be lessening potential harmful effects that disclosure may have on an individual. Before genetic testing can be offered on a clinical basis, these issues need to be addressed so that we can be prepared to offer appropriate genetic counseling and medical management [Lerman et al., 1991].

We were in a unique position at the University of Minnesota to examine the perceptions of individuals after notification of a family history of breast cancer. Beginning in 1993, a follow-up study of 544 breast cancer families was begun at the University of Minnesota [Sellers et al., 1995]. Early in the course of the study, hereafter referred to as the large follow-up study, some participants independently contacted the study personnel with specific concerns about the notification process [Wiesner et al., 1993]. In some cases, individuals were unaware of a family history of breast cancer. Others questioned the manner in which they were contacted. Therefore, we embarked on a systematic study to explore the impact of notification of a family history of breast cancer on these family members. We wished to define the proportion of family members that were knowledgeable about their family history, assess reasons for participation, and evaluate issues of privacy and confidentiality in this cohort.

METHODS

Study Families

In 1944, a case-control family study was initiated at the University of Minnesota to investigate the influences of childbearing, breastfeeding, and positive family history on the occurrence of breast cancer [Anderson et al., 1958]; 544 index cases with breast cancer from the state of Minnesota were ascertained between 1938 and 1952 at the Tumor Clinic without prior knowledge of their family history. A large follow-up study of these families is currently being conducted [Sellers et al., 1995]. Eligible participants include first- and second-degree female relatives of probands (blood relatives) and female spouses of probands' first- and second-degree male relatives (marry-ins). Data on disease status and cancer risk factors are collected by a combination of telephone interviews, mailed questionnaires, and medical records reviews.

To initiate the process of updating and extending the pedigrees from the 1944 baseline study, at least one individual had to be identified from each family. This initial contact person was located using the last known address of family members, telephone directories, directory assistance operators, and reverse directories. Once located, the individual was contacted by telephone to verify family membership and mailed a letter explaining the study. A staff member then called the initial contact person for the pedigree extension interview. If the initial contact was unable to provide information for all family members, another relative was called without an introductory letter and asked for assistance. The number of individuals contacted per family during pedigree extension was dependent on the family size, geographic location, and whether family members communicated regularly.

Notification Questionnaire

One hundred sixty consecutive families were surveyed with the notification questionnaire by telephone interview from April 30, 1993 to March 3, 1994. Up to five contacts, or all if less than five, in each family were randomly interviewed at the conclusion of the pedigree extension interview without regard to gender or relationship to the proband. The survey consisted of five questions, four of which were open-ended to facilitate unbiased responses. Questions were designed to assess 1) each contact's prior knowledge of his or her family history of breast cancer, 2) reasons for and 3) concerns about participating in the follow-up study, and 4) personal concerns about developing cancer. The fifth question permitted each respondent an opportunity to contribute any additional personal or family information that he or she felt was relevant. For each respondent the name, relationship to the proband (via family identification number) and gender was recorded. Age was recorded only for those respondents who were eligible for follow-up in the large follow-up study (i.e., first- or second-degree female relatives or spouses of first- or second-degree male relatives).

In order to assess whether the survey was representative of this cohort's overall concerns for privacy and confidentiality, individuals from 53 consecutive families were monitored for spontaneous comments during the pedigree extension interview and/or administration of the notification questionnaire. Concerns about participation expressed during the notification survey were considered separately from all other spontaneous comments. Staff members noted all spontaneous or unsolicited comments about privacy or confidentiality issues, the nature of the comments, and the gender and degree of relationship of the participant to the proband.

Data Analysis

Responses to each question were reviewed and assigned to logical categories. One respondent was excluded from analysis due to incomplete personal information. Statistical evaluation of the data was performed by means of contingency table analyses. In addition, the specific cases who independently contacted study personnel were excluded from the analysis.

TABLE I. Gender and Biological Relationship of 376 Family Members Surveyed With the Notification Questionnaire

	Frequency (n)	Percent (%)
Gender		
Male	78	21
Female	298	79
Degree of relationship to proband		
Blood relative (total)	308	82
Proband	2	1
Sibling	7	2
Child	73	19
Grandchild	45	12
Niece/nephew	140	37
Third degree/distant	41	11
Non-blood relative	68	18

RESULTS

Most of the 376 respondents were female and biologically related to the proband (Table I). Among blood relatives, 21% were first-degree relatives (children and sisters) and 49% were second-degree relatives (grandchildren, nieces, nephews). Non-blood relatives included all individuals who had married into the family (marry-ins), caregivers for family members, adopted relatives, or "step-" relatives. The mean age of 258 blood relatives for whom age was recorded was 66.0 years, as compared with the mean age of 64.4 years for 65 non-blood relatives. A fraction of those interviewed (26%) were unaware of their family history, with little difference observed based on the gender of the respondent (Table II). As expected, blood relatives were significantly more likely than non-blood relatives to be aware of a family history of breast cancer on the proband's side of the family (77% vs. 62%, $P < 0.01$), and those who were less closely related to the proband were less likely to be aware of a family history of breast cancer. Among children of probands, the proportion of sons and daughters that reported awareness were similar (100% and 94%, respectively). However, female second-degree relatives (77% of granddaughters and 77% of nieces) were more aware of the breast cancer history than their male counterparts (64% of grandsons and 62% of nephews).

Motivation for participation in the larger follow-up study was given by 375 respondents (429 total responses). Eleven categories were defined (Table III), with the vast majority of responses (73%) classified as "general or altruistic" reasons. While a higher proportion of women than men stated a specific reason for participating (13% vs. 5%, $P = 0.04$), all other responses were similar for men and women. A history of cancer in relatives, close friends, or the participants themselves was cited by 54 (15%) respondents as a reason for participating, but there was no significant difference between individuals who were previously aware of their family history and those who were unaware. A similar proportion of blood (12%) and non-blood relatives (10%) stated that family history was a reason to enter the large follow-up study. Among blood relatives, 29% of siblings (n = 2), 16% of children (n = 12), and 12% of distant relatives (n = 5) cited family history of cancer compared to only 9% of nieces and nephews (n = 13) and 9% of grandchildren (n = 4).

A total of 366 individuals responded to an open-ended question regarding additional participation concerns; the majority (88%) had no comments (Table II). There was little difference in the frequency of concerns by gender or biological relationship to the proband. Of 301 responding blood relatives, 33 (11%) had participation concerns compared to 15% of 65 responding non-blood relatives. The 43 specific participation issues fell into two broad categories: worries about the amount of time and level of effort required (n = 27) and concerns regarding privacy or confidentiality (n = 16). The majority of individuals with either concerns about effort and time (n = 19, 70%) or privacy and confidentiality (n = 14, 88%) were aware of a family history of breast cancer. In addition, six respondents who agreed to complete the notification survey refused to participate in the large follow-up study. The reasons for refusal were primarily about time and effort rather than privacy.

The level of concern about developing cancer was high in all groups (Table II). Interestingly, the concern was as

TABLE II. Knowledge of Family History, Participation Concerns, and Concerns About Cancer by Gender and Relationship to the Proband in Family Members of 160 Breast Cancer Probands

	Aware of family history (n = 375)		Participation concern (n = 366)		Concern about developing cancer (n = 372)	
	(n)	(%)	(n)	(%)	(n)	(%)
Gender						
Male	58	75	9	12	50	66
Female	218	73	34	12	193	65
Degree of relationship to proband						
Blood relative	234	76	33	11	203	67
Proband	2	100	1	50	1	50
Sibling	7	100	1	17	5	71
Child	70	96	8	11	57	78
Grandchild	33	73	3	7	33	73
Niece/nephew	103	74	17	13	76	55
Third degree/distant	19	46	3	7	31	78
Non-blood relative	42	62	10	15	40	60

TABLE III. Distribution of Motives Given by 375 Family Members for Their Participation in a Genetic Epidemiologic Study of Breast Cancer

Motivation	Frequency (n) (n = 429)[a]	Percent (%)[b]
General/altruistic	274	73.1
Family history of cancer	43	11.5
Seriousness of cancer/ media coverage/ health professional	21	5.6
Another relative is participating	16	0.4
To gain knowledge about breast cancer	15	4.0
Good reputation of University of Minnesota	13	3.5
Personal history of cancer	7	1.9
Close friend had cancer	4	1.1
Family history of another disease	4	1.1
No reason specified	26	6.9
Refused participation in genetic epidemiological study	6	1.6

[a] Number of responses is greater than participants because of multiple responses from some participants.
[b] Percents may not sum to 100% because of multiple responses from some participants.

high in male as in female respondents, and non-blood relatives were only slightly less concerned than blood relatives. When asked "Is the possibility of getting cancer a health concern for you and your family?", 358 individuals answered with one comment and 15 individuals offered two (Table IV). The most frequent comment involved a general level of concern with statements such as "everyone should be concerned" and "I'm aware of it, but I don't dwell on it." Prior knowledge of their family history of cancer (15%) or personal history of cancer (6%) were cited infrequently. Additional analyses were performed to assess whether the degree of biological relatedness or prior knowledge of a family history of cancer was associated with an increase in anxiety about developing cancer. Interestingly, the level of concern expressed by the proportion of third-degree or more distant relatives was similar to if not greater than the proportion of first- and second-degree relatives (Table II). While the number of cancer concerns expressed by sons (77%) and daughters (79%) was similar, 82% of granddaughters (n = 28) and only 46% of grandsons (n = 5) reported being concerned. Furthermore, prior knowledge of family history of cancer was unrelated to concern (76% vs. 69%, $P = 0.14$). Similar comparison of family history awareness and cancer concern by gender revealed no significant differences. We wondered whether concern about developing cancer would have an impact on an individual's decision to enter the study. Respondents who expressed such concern were somewhat less likely to have specific issues about participating in the larger follow-up study than individuals without cancer concerns (10% vs. 15%, $P < 0.15$).

In order to determine the level of concern for issues relating to privacy or confidentiality, the interviews for 53 families were monitored for unsolicited comments. There were a total of 630 contacts in 53 consecutive interviews to extend family pedigrees. Only 19 individuals (3%) in 15 families expressed some concern about privacy. Seven comments occurred during the administration of the notification questionnaire, and 12 (2%) were spontaneously offered in the pedigree extension interview. Frequency of privacy concerns did not vary by gender or relationship to the proband. The specific content of six spontaneous concerns (50%) compared to a total of eleven questionnaire-assessed concerns (69%) involved general unwillingness to provide personal information over the phone. Comments addressing family dynamics or sensitivity for the privacy of a particular relative were spontaneously offered by one son, two grandchildren, two third-degree relatives, and one non-blood family member. Two male relatives spontaneously asked whether their relatives' or their own names and addresses would be made commercially available for companies to send unsolicited advertise-

TABLE IV. Distribution of Responses by 373 Family Members to Open-Ended Questions About Cancer Concerns

Comment	Frequency (n)[a] (n = 388)	Percent (%)[b]
General concern	121	32.4
Health issues (regular checkups, healthy lifestyle)	71	19.0
Family history of cancer	55	14.7
Personal history of cancer	21	5.6
Family history of another disease	13	3.5
Widespread media coverage of cancer	7	1.9
Privacy issue (insurance)	1	0.3
No concern specified	99	26.5

[a] Three participants declined to respond to this question and 15 offered 2 responses.
[b] % may not sum to 100% because of multiple responses from some participants.

ments. During administration of the notification questionnaire, two male respondents expressed concern about the release of data to insurance agencies.

DISCUSSION

This report describes the impact of notification of a family history of breast cancer on 376 members of 160 families originally ascertained by a single proband with breast cancer. Nearly one quarter of our cohort was unaware of a family history of cancer prior to contact by our study. We had hypothesized that notification of a family history might increase an individual's perception of his or her risk for developing cancer and lead to a higher level of anxiety. If this were true, we would have expected to see a greater level of concern in blood relatives who had previously been unaware of their family history; such an outcome was not observed.

An unexplainably high proportion of third-degree or more distant relatives expressed concern about developing cancer. One may question whether the cancer concern indicated by participants in this study stems from their family history, as spontaneously suggested by 55 respondents, or whether the increasing role of the media in promoting cancer screening is the primary influence, as mentioned by 7 respondents. Furthermore, a respondent's perception of a family history of cancer may be substantially different from this study's definition of family history (a diagnosis of breast cancer in the proband). A small number of respondents clearly indicated awareness of the proband's diagnosis but expressed the opinion that they did not have a history of breast cancer in their family.

There was essentially no difference between the proportion of males and females who expressed concern about developing cancer. However, it is unclear whether the men who expressed a cancer concern were more worried about their own health or about the health of their female relatives. Little research exists on cancer risk perception among male relatives of breast cancer patients. Many studies have demonstrated that female relatives, especially daughters, of breast cancer patients tend to greatly overestimate their risk of developing breast cancer [Biesecker et al., 1993; Lynch et al., 1993; Wellisch et al., 1991], while other women at high risk for breast cancer greatly underestimate their risk [Lynch et al., 1993; Thirlaway and Fallowfield, 1993; Kash et al., 1992]. Evans et al. [1993] found that a woman's personal estimation of developing breast cancer increases with significance of family history. Our results indirectly support this finding because the nieces and non-blood relatives in our sample reported a lower frequency of cancer concern than first-degree relatives and granddaughters. However, we did not ask the participants to estimate their risk or specify a level of concern.

We were interested in the potential impact that notification might have on participation in the study and on the respondents' perceptions of privacy. Participants who had no previous knowledge about a family history of breast cancer might have been expected to have more privacy issues or concerns about entering the study; our data do not support this premise. Unexpectedly, most of the privacy concerns were expressed by participants already aware of their family history, and it was encouraging to find a small number of privacy concerns among individuals newly notified of their family history of breast cancer. The majority of individuals who expressed concerns were skeptical of sharing personal information over the telephone with unknown callers. Other worries involved fear of adverse personal consequences associated with insurance companies or receiving "junk mail." Very few privacy concerns dealt with personal feelings, overt suspicion, or the privacy or feelings of other family members. Thus, if privacy concerns were raised by notification in our epidemiologic research context, such concerns were not necessarily overt or immediate.

The ethical issues encountered with the disclosure of a family history of breast cancer are complex because notification could have a negative impact on the individual at a higher risk for developing cancer [Lerman et al., 1991]. However, the initial effect of notification on the 376 family members of 160 breast cancer families was minimal in this study. We found no evidence for a detrimental effect of notification when we analyzed the responses from the individuals who were unaware of their family history. While results of our study are encouraging regarding the initial responses following notification, the results should be interpreted cautiously. First, the response to notification of a family history of cancer in a distant relative could be quite different from the notification that a close relative is carrying a known cancer-predisposing gene. Second, the sample of families studied were not selected on the basis of a strong family history of breast cancer, merely through a single proband with the disease. Thus, only a minority of the families will ultimately be shown to be "hereditary." Future studies should address the potential long term effects of notification by monitoring behavioral responses to cancer screening after disclosure. In addition, the psychosocial effects of notification should be included in future studies of the impact of notification on individuals at genetic risk for cancer.

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REFERENCES

American Society of Human Genetics Ad Hoc Committee (1994): ASHG policy statement on genetic testing for breast and ovarian cancer predisposition. Am J Hum Genet 55:i–iv.

Anderson V, Goodman H, Reed S (1958): "Variables Related to Human Breast Cancer." Minneapolis, Minnesota: The University of Minnesota Press.

Biesecker B, Boehnke M, Calzenek K, Markel D, Garber J, Collins F, Weber B (1993): Genetic counseling for families with inherited susceptibility to breast and ovarian cancer. JAMA 269:1970–1974.

Caplan A (1992): Mapping Mortality: Ethics and the Human Genome Project: "If I Were a Rich Man Could I Buy a Pancreas?" Indiana University Press, pp 118–142.

Evans D, Burnell L, Hepwood P, Howell A (1993): Perception of risk in women with a family history of breast cancer. Br J Cancer 67: 612–614.

Harris J, Lippman M, Veronesi U, Willet W (1992): Breast cancer (first of three parts). N Engl J Med 327:319–328.

Kash K, Holland J, Halper M, Miller D (1992): Psychological distress and surveillance behaviors of women with a family history of breast cancer. J Natl Cancer Instit 84:24–30.

King M, Rowell S, Love S (1993): Inherited breast and ovarian cancer: What are the risks? What are the choices? JAMA 269:1975–1980.

Lerman C, Rimer B, Engstrom P (1991): Cancer risk notification: Psychosocial and ethical implications. J Clin Oncol 9:1275–1282.

Lynch H, Watson P, Conway T, Lynch J, Slominski-Caster S, Narod S, Feunteun J, Lenoir G (1993): DNA screening for breast/ovarian cancer susceptibility based on linked markers. Arch Int Med 153: 1979–1987.

Miki Y, Swensen J, Shattuck-Eidens D, Futreal PA, Harshman K, Tavtigian S, Liu Q, Cochran C, Bennett LM, Ding W, Bell R, Rosenthal J, Hussey C, Tran T, McClure M, Frye C, Hattier T, Phelps R, Haugen-Strano A, Katcher H, Yakumo K, Gholami Z, Shaffer D, Stone S, Bayer S, Wray C, Bogden R, Dayananth P, Ward J, Tonin P, Narod S, Bristow PK, Norris FH, Helvering L, Morrison P, Rosteck P, Lai M, Barrett JC, Lewis C, Neuhausen S, Cannon-Albright L, Goldgar D, Wiseman R, Kamb A, Skolnick MH (1994): A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1. Science 266:66–71.

Motulsky, A (1994): Predictive genetic diagnosis. Am J Hum Genet 55:603–605.

Sellers T, Anderson V, Potter J, Bartow S, Chen P, Everson L, King R, Kuni C, Kushi L, McGovern P, Rich S, Whitbeck J, Wiesner G (1995): Epidemiologic and genetic study of 544 Minnesota Breast Cancer Families: Design and methods. Genet Epidemiol 12: 417–429.

Thirlaway K, Fallowfield L (1993): The psychological consequences of being at risk of developing breast cancer. Eur J Cancer Prevention 2:467–471.

Wellisch D, Gritz E, Schain W, Wang H, Siau J (1991): Psychological functioning of daughters of breast cancer patients: Part I: Daughters and comparison subjects. Psychosomatics 32:324–336.

Wiesner GL, Winter R, Bartels D, Sellers TA, LeRoy BS (1993): Complex issues encountered with the disclosure of a family history of breast cancer. Am J Hum Genet 53:1511 (abstract).

Wooster R, Neuhausen SL, Mangion J, Quirk Y, Ford D, Collins N, Nguyen K, Seal S, Tran T. Averill D, Fields P, Marshall G, Narod S, Lenoir GM, Lynch H, Feunteun J, Devilee P, Cornelisse CJ, Menko FH, Daly PA, Ormiston W, McManus R, Pye C, Lewis CM, Cannon-Albright L, Peto J, Ponder BAJ, Skoinick MH, Easton DF, Goldgar DE, Stratton MR (1994): Localization of a breast cancer susceptibility gene, BRCA2, to chromosome 13q12-13. Science 265:2088–2090.